

**Division of Medical Assistance
Genotyping and Phenotyping
for HIV Drug Resistance Testing**

**Clinical Coverage Policy No.: 1S-1
Original Effective Date: July 1, 1996**

**DRAFT
Table of Contents**

1.0	Description of Services	1
1.1	Human Immunodeficiency Virus Drug Resistance Testing	1
1.2	Genotype Tests	1
1.3	Phenotype Tests	1
1.4	Viral Load	1
1.5	Antiretroviral Therapy	2
1.6	Adherence	2
1.7	Regimen Failure.....	2
2.0	Eligible Recipients	2
2.1	General Provisions	2
2.2	EPSDT Special Provision: Exception to Policy Limitations for Recipients under 21 Years of Age	2
3.0	When the Service Is Covered.....	3
3.1	General Criteria.....	3
3.2	Specific Criteria	4
4.0	When the Service Is Not Covered.....	4
4.1	General Criteria.....	4
4.2	Specific Criteria	4
5.0	Requirements for and Limitations on Coverage	5
5.1	Prior Approval	5
5.2	Testing Requirements	5
5.3	Limitations	6
6.0	Providers Eligible to Bill for Services	6
7.0	Additional Requirements	6
7.1	Federal and State Requirements.....	6
7.2	Hospital Inpatient Testing.....	7
7.3	Records Retention.....	7
8.0	Policy Implementation/Revision Information.....	7
	Attachment A: Claims-Related Information	8

DRAFT

1.0 Description of Services

1.1 Human Immunodeficiency Virus Drug Resistance Testing

Human Immunodeficiency Virus (HIV) is a ribonucleic acid (RNA) virus characterized by a high replication rate throughout all stages of infection. There are four types of HIV: HIV-1, HIV-2, Human T-cell Lymphotropic Virus (HTLV) type 1, and HTLV type 2. This policy addresses only HIV-1. In HIV-1, the reverse transcription enzyme required for replication is error prone, resulting in a high rate of mutations. Viral replication continues in the presence of the selective drug(s). This is called drug resistance, and it is one of the most common reasons for failure of HIV therapy.

HIV drug resistance testing assesses the HIV strain(s) infecting an individual to determine each strain's resistance to specific antiretroviral drugs. Two methods are available for testing resistant HIV strains: genotypic and phenotypic. Both isolate the virus from the patient. Genotype tests detect specific mutations in the genome of a patient's viral isolate that are associated with antiretroviral resistance. Phenotype tests assess how well the patient's virus grows in the presence of different concentrations of antiretroviral drugs and compares these concentrations with a viral strain used as a control.

1.2 Genotype Tests

Genotype tests look for genetic mutations that have been linked to a drug's resistance. Genotypic tests are performed by directly testing for specific mutations, but will only detect the mutations in the predominant strain of virus. Resistant mutations in minor viral strains will not be detected in a genotype. Genotype testing is faster and easier to perform than phenotype testing. It can be performed at significantly lower cost, and is more widely available throughout the United States. Standard genotype testing may not be able to be performed in individuals with HIV RNA < 1000 copies/ml.

1.3 Phenotype Tests

Phenotype tests assess which drugs can stop HIV from growing in a laboratory setting. They measure a virus's ability to grow in different concentrations of antiretroviral drugs and the ability of drugs to block viral replication in cell culture. Disadvantages of phenotypic testing are considerable delay of reporting time due to the wait for culture growth, insensitivity to minor viral species, and relative expense.

1.4 Viral Load

Viral load is the amount of HIV RNA in a blood sample, reported as the number of HIV RNA copies per milliliter of blood plasma. The viral load provides information about the amount of HIV that is replicating in the blood plasma but is not indicative of the amount of HIV contained within cells. HIV RNA can be used in conjunction with other variables in predicting HIV progression and in determining how effectively antiretroviral therapy (ART) is working.

DRAFT

1.5 Antiretroviral Therapy

An antiretroviral drug is a substance that stops or suppresses the activity of a retrovirus such as HIV. *Antiviral* is sometimes used as an alternate term. Examples of antiretroviral drugs are zidovudine (AZT, brand name Retrovir), abacavir (ABC, brand name Ziagen), and tenofovir (TDF, brand name Viread). Antiretroviral drugs interfere with HIV replication to delay disease progression.

1.6 Adherence

Adherence is the degree to which a patient exactly follows a prescribed treatment regimen. *Compliance* is an alternate term.

1.7 Regimen Failure

Regimen failure occurs when the anti-HIV medications being taken do not adequately control viral replication. Factors that may cause regimen failure include, but are not limited to, the following:

- a. Poor health before starting the treatment regimen
- b. Poor adherence to the regimen (not taking medications exactly as instructed by a provider; missing doses)
- c. Previous HIV treatment and/or drug resistance
- d. Alcohol or drug abuse
- e. Medication side effects, medication toxicity, or interactions with other medications
- f. Medication poorly absorbed by the body (pharmacokinetic issues)
- g. Medical conditions or illnesses other than HIV infection

2.0 Eligible Recipients

2.1 General Provisions

Medicaid recipients may have service restrictions due to their eligibility category that would make them ineligible for this service.

2.2 EPSDT Special Provision: Exception to Policy Limitations for Recipients under 21 Years of Age

42 U.S.C. § 1396d(r) [1905(r) of the Social Security Act]

Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) is a federal Medicaid requirement that requires the state Medicaid agency to cover services, products, or procedures for Medicaid recipients under 21 years of age **if** the service is **medically necessary health care** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem] identified through a screening examination** (includes any evaluation by a physician or other licensed clinician). This means EPSDT covers most of the medical or remedial care a child needs to improve or maintain his/her health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems. Medically necessary services will be provided in the most economic mode, as long as the treatment made available is similarly efficacious to the service requested by the recipient's physician, therapist, or

DRAFT

other licensed practitioner; the determination process does not delay the delivery of the needed service; and the determination does not limit the recipient's right to a free choice of providers.

EPSDT does not require the state Medicaid agency to provide any service, product, or procedure:

- a. that is unsafe, ineffective, or experimental/investigational.
- b. that is not medical in nature or not generally recognized as an accepted method of medical practice or treatment.

Service limitations on scope, amount, duration, frequency, location of service, and/or other specific criteria described in clinical coverage policies may be exceeded or may not apply as long as the provider's documentation shows that the requested service is medically necessary "to correct or ameliorate a defect, physical or mental illness, or a condition" [health problem]; that is, provider documentation shows how the service, product, or procedure will correct or improve or maintain the recipient's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

****EPSDT and Prior Approval Requirements**

- a. If the service, product, or procedure requires prior approval, the fact that the recipient is under 21 years of age does **NOT** eliminate the requirement for prior approval.
- b. **IMPORTANT ADDITIONAL INFORMATION** about EPSDT and prior approval is found in the *Basic Medicaid Billing Guide*, sections 2 and 6, and on the EPSDT provider page. The Web addresses are specified below.

Basic Medicaid Billing Guide: <http://www.ncdhhs.gov/dma/medbillcaguide.htm>

EPSDT provider page: <http://www.ncdhhs.gov/dma/EPSDTprovider.htm>

3.0 When the Service Is Covered

IMPORTANT NOTE: EPSDT allows a recipient less than 21 years of age to receive services in excess of the limitations or restrictions below and without meeting the specific criteria in this section when such services are **medically necessary health care services** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem]; that is, documentation shows how the service, product, or procedure will correct or improve or maintain the recipient's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

EPSDT DOES NOT ELIMINATE THE REQUIREMENT FOR PRIOR APPROVAL IF PRIOR APPROVAL IS REQUIRED. For additional information about EPSDT and prior approval requirements, see **Section 2.0** of this policy.

3.1 General Criteria

Medicaid covers genotype and phenotype testing for HIV drug resistance when the service is medically necessary and

- a. the procedure is individualized, specific, and consistent with symptoms or confirmed diagnosis of the illness or injury under treatment, and not in excess of the recipient's needs;

DRAFT

- b. the procedure can be safely furnished, and no equally effective and more conservative or less costly treatment is available statewide; and
- c. the procedure is furnished in a manner not primarily intended for the convenience of the recipient, the recipient's caretaker, or the provider.

3.2 Specific Criteria

Genotype and phenotype testing for HIV drug resistance is considered medically necessary when either process is used to assist in the selection of a new treatment regimen. A new regimen may be necessary if the recipient has experienced *any* of the following:

- a. virologically failed the prescribed regimen; or
- b. achieved a suboptimal response after the initiation of ART (optimal response is defined as reduction of plasma HIV RNA to less than 50 copies/ml); or
- c. has been found to have acute HIV infection; or
- d. has been infected with HIV for less than 12 months; or
- e. is initiating the first ART regimen regardless of duration of infection; or
- f. is pregnant and has detectable HIV RNA in plasma.

Genotype or phenotype testing is recommended prior to changing therapy for treatment failure. Resistance assays should be obtained when patients have a viral load greater than 1,000 copies/ml and are still on the failing regimen.

4.0 When the Service Is Not Covered

IMPORTANT NOTE: EPSDT allows a recipient less than 21 years of age to receive services in excess of the limitations or restrictions below and without meeting the specific criteria in this section when such services are **medically necessary health care services** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem]; that is, documentation shows how the service, product, or procedure will correct or improve or maintain the recipient's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

EPSDT DOES NOT ELIMINATE THE REQUIREMENT FOR PRIOR APPROVAL IF PRIOR APPROVAL IS REQUIRED. For additional information about EPSDT and prior approval requirements, see **Section 2.0** of this policy.

4.1 General Criteria

The service is not covered when

- a. the recipient does not meet the eligibility requirements listed in **Section 2.0**;
- b. the recipient does not meet the medical necessity criteria listed in **Section 3.0**;
- c. the procedure unnecessarily duplicates another provider's procedure; or
- d. the procedure is experimental, investigational, or part of a clinical trial.

4.2 Specific Criteria

Genotype and phenotype testing for HIV drug resistance is not covered in the following circumstances.

- a. The viral load is fewer than 1,000 copies/ml.

DRAFT

- b. Combined genotype and phenotype testing for HIV drug resistance is considered investigational, but could be considered medically necessary in a complex case where the physician believes both types of testing might provide additional useful information, not provided by one or the other. This will be determined on a case-by-case basis, and with medical documentation supporting why both tests are necessary.

5.0 Requirements for and Limitations on Coverage

IMPORTANT NOTE: EPSDT allows a recipient less than 21 years of age to receive services in excess of the limitations or restrictions below and without meeting the specific criteria in this section when such services are **medically necessary health care services** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem]; that is, documentation shows how the service, product, or procedure will correct or improve or maintain the recipient's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

EPSDT DOES NOT ELIMINATE THE REQUIREMENT FOR PRIOR APPROVAL IF PRIOR APPROVAL IS REQUIRED. For additional information about EPSDT and prior approval requirements, see **Section 2.0** of this policy.

5.1 Prior Approval

Prior approval is not required.

5.2 Testing Requirements

The following are based on Medicare national coverage decisions.

- a. Viral quantification may be appropriate for prognostic use, including baseline determination, periodic monitoring, and monitoring of response to therapy. Use as a diagnostic test method is not indicated.
- b. Measurement of plasma HIV RNA levels should be performed at the time of establishment of an HIV infection diagnosis. For an accurate baseline, two specimens in a 2-week period are appropriate.
- c. For prognosis including ART monitoring, regular, periodic measurements are appropriate. The frequency of viral load testing should be consistent with the most current Centers for Disease Control and Prevention (www.cdc.gov/hiv) guidelines for use of antiretroviral agents in adults and adolescents and pediatric HIV infection.
- d. Because different assays can produce apparent differences in absolute HIV copy number, plasma HIV RNA levels should be measured by the same analytical method each time testing is done if possible. A change in assay method may necessitate re-establishment of a baseline.
- e. In pregnant women, the purpose of ART is to reduce plasma HIV RNA to less than the limit of detection, for the benefit of both mother and child. Genotypic resistance testing is recommended for all pregnant women prior to initiation of therapy and for those entering pregnancy with detectable HIV RNA level while on therapy. Optimal prevention of perinatal transmission may require initiation of ART before results of resistance testing are available.

DRAFT

- f. In neonates, early diagnostic testing for the detection of HIV-1 infection should be done in order for treatment to be initiated as soon as possible. The optimal prophylactic regimen for newborns of women with antiretroviral resistance is unknown. Therefore, antiretroviral prophylaxis for an infant born to a woman with known or suspected drug resistance should be determined in consultation with a pediatric HIV specialist, preferably before delivery.
- g. In children (birth through age 16), antiretroviral drug resistance testing is recommended before initiating therapy in all treatment-naïve children and before changing therapy for treatment failure. Resistance assays should be obtained when patients have a viral load greater than 1,000 copies/ml and are still on the failing regimen or within four weeks of discontinuation of the regimen. Consultation with a specialist in pediatric HIV infection is recommended for interpretation of resistance assays when considering starting or changing an antiretroviral regimen in a pediatric patient.
Note: Adult guidelines are usually appropriate for post-pubertal adolescents.
- h. The test must be ordered by a treating physician or other qualified treating non-physician practitioner within the scope of their license and in compliance with Medicaid requirements.

5.3 Limitations

The following are based on Medicare national coverage decisions.

- a. Coverage is limited to no more than two HIV-1 drug-resistant tissue tests (CPT codes 87903 and 87904) in a 12-month period.
- b. There are circumstances in which both a genotype and a phenotype test need to be obtained at the same time. If additional testing is needed within a 12-month period, an exception may be requested. Requests for exemptions are reviewed on an individual basis, and may be requested by contacting Electronic Data Services (EDS) at 800-688-6696 or 919-851-8888. Requests must include medical necessity documentation.

6.0 Providers Eligible to Bill for Services

Laboratories and other providers who have been approved to perform HIV drug resistance testing under a valid Clinical Laboratory Improvement Amendment (CLIA) permit in the category of HIV testing issued by the Centers for Medicare and Medicaid Services are eligible to bill for the service when

- a. they meet Medicaid's qualifications for participation;
- b. they are currently enrolled with the N.C. Medicaid program; and
- c. the service is within the scope of their practice.

7.0 Additional Requirements

7.1 Federal and State Requirements

Providers must comply with all applicable federal and state laws and regulations.

DRAFT

7.2 Hospital Inpatient Testing

Medicaid payment to the hospital includes all necessary laboratory services.

7.3 Records Retention

As a condition of participation, providers are required to keep records necessary to disclose the extent of services rendered to recipients and billed to the N.C. Medicaid program [Social Security Act 1902(a)(27) and 42 CFR 431.107]. Records must be retained for a period of at least five years from the date of service, unless a longer retention period is required by applicable federal or state law, regulations, or agreements (10A NCAC 22F.0107).

Copies of records must be furnished upon request.

The Health Insurance Portability and Accountability Act (HIPAA) does not prohibit the release of records to Medicaid (45 CFR 164.502).

8.0 Policy Implementation/Revision Information

Original Effective Date: July 1, 1996

Revision Information:

Date	Section Revised	Change

DRAFT

Attachment A: Claims-Related Information

Reimbursement requires compliance with all Medicaid guidelines, including obtaining appropriate referrals for recipients enrolled in the Medicaid managed care programs.

A. Claim Type

Professional (CMS-1500/837P transaction)

Institutional (UB-04/837I transaction)

B. Diagnosis Codes

Providers must bill the ICD-9-CM diagnosis codes(s) to the highest level of specificity that supports medical necessity.

ICD-9 Codes

ICD-9-CM Diagnosis Code	Description
042	Human immunodeficiency virus [HIV] disease
079.53	Retrovirus; Human immunodeficiency virus, type 2 [HIV-2]
795.71	Other nonspecific immunological findings; Nonspecific serologic evidence of human immunodeficiency virus [HIV]
V08	Asymptomatic human immunodeficiency virus [HIV] infection status

C. Procedure Codes

CPT Code	Description
87536	Infectious agent detection by nucleic acid (DNA or RNA); HIV-1, quantification
87539	Infectious agent detection by nucleic acid (DNA or RNA); HIV-2, quantification
87900	Infectious agent drug susceptibility phenotype prediction using regularly updated genotypic bioinformatics
87901	Infectious agent genotype analysis by nucleic acid (DNA or RNA); HIV 1, reverse transcriptase and protease
87903	Infectious agent phenotype analysis by nucleic acid (DNA or RNA) with drug resistance tissue culture analysis, HIV 1; first through 10 drugs tested
87904	Infectious agent phenotype analysis by nucleic acid (DNA or RNA) with drug resistance tissue culture analysis, HIV1; each additional drug tested (List separately in addition to code for primary procedure)

DRAFT

Component Lab Codes listed below cannot be billed on the same date of service as CPT codes 87901, 87903, and 87904.

CPT Code	Description
83890	Molecular diagnostics; molecular isolation or extraction
83894	Molecular diagnostics; separation by gel electrophoresis (eg. agarose, polyacrylamide).
83898	Molecular diagnostics; amplification, target, each nucleic acid sequence
83902	Molecular diagnostics; reverse transcription
83904	Molecular diagnostics; mutation identification by sequencing, single segment, each segment
83912	Molecular diagnostics; interpretation and report
87252	Virus isolation; tissue culture inoculation, observation, and presumptive identification by cytopathic effect
87253	Virus isolation; tissue culture, additional studies or definitive identification (eg, hemabsorption, neutralization, immunofluorescence stain), each isolate

D. Modifiers

Providers are required to follow applicable modifier guidelines.

E. Billing Units

One unit = 1 HIV drug-resistant tissue culture test; up to a maximum of two units per 12 months per patient.

F. Place of Service

Inpatient, outpatient, physician's office

G. Co-Payments

HIV genotyping and phenotyping are not subject to co-payments.

H. Reimbursement

Providers must bill their usual and customary charges.

Note: Fees for specimen drawing or collecting and handling of laboratory specimens are allowed only if the laboratory test for which the specimen was obtained is not performed in the physician's office.

I. Billing Guidelines

CPT 86701 or 86703 is performed initially.

CPT 86702 is performed when the results of 86701 are negative and clinical suspicion of HIV-2 exists.

CPT 86689 is performed only on samples that show repeated positive results by 86701, 86702, or 86703.

Note: Medicaid requires the laboratory performing the test(s) to bill for the service.